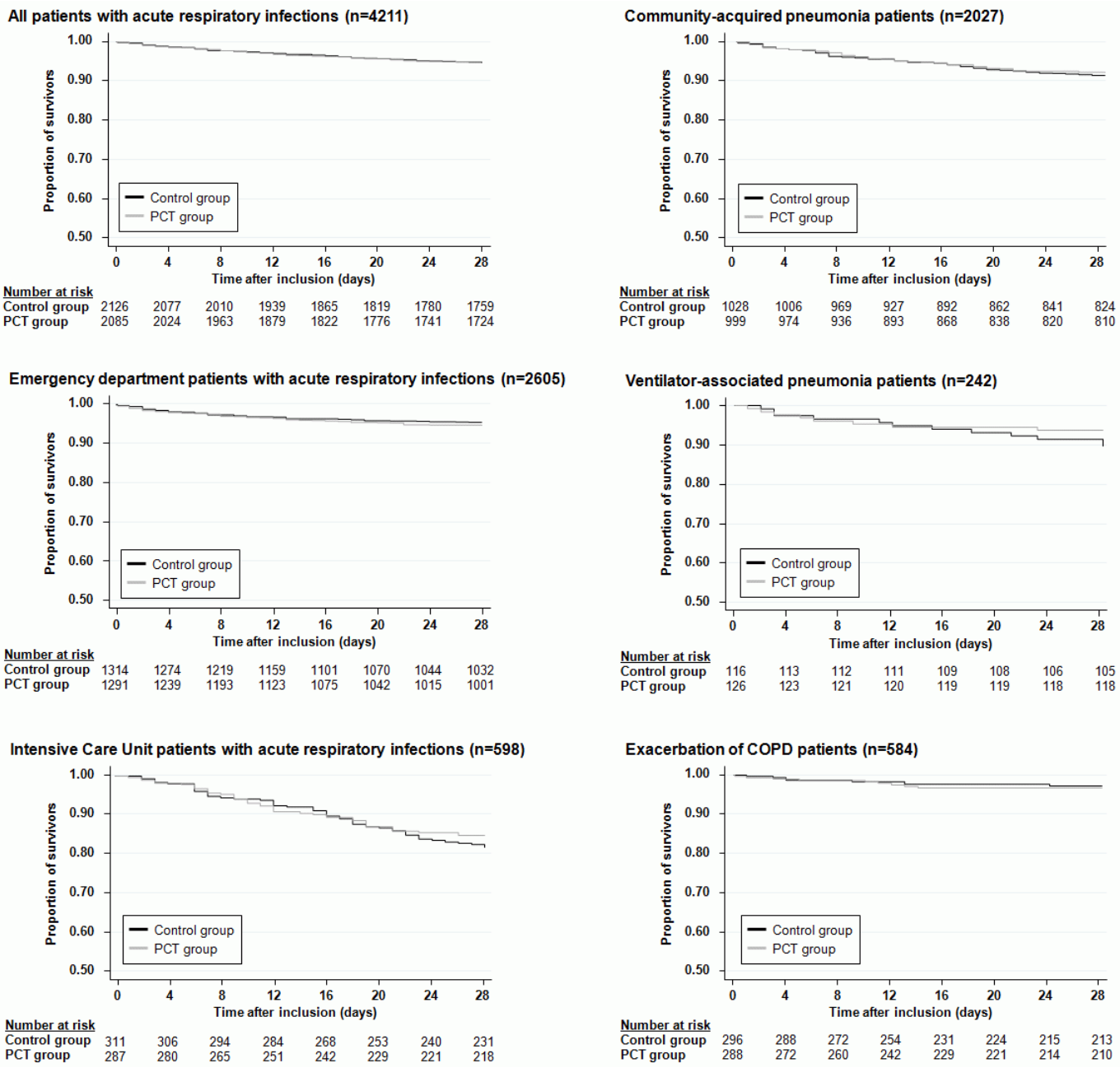
Extra web appendix 1. Definition of ARI subtype

ARI subtype	Definition
Upper respiratory infection	Clinical diagnosis of common cold, rhinosinusitis, pharyngitis, tonsillitis, otitis media or other unspecific upper respiratory infection; no additional diagnostic tests required. Definitions were similar among the two primary care trials.
Lower respiratory tract infection	Presence of at least one respiratory symptom (cough, sputum production, dyspnea, tachypnea, pleuritic pain) plus at least one finding during auscultation (rales, crepitation), or one sign of infection (core body temperature >38.0°C, shivering, leukocyte count >10`000cells/uL or <4`000cells/uL) independent of antibiotic pre-treatment
Acute bronchitis	Lower respiratory tract infection without infiltrate in the absence of an underlying lung disease or focal chest signs and infiltrates on chest X-ray
Community-acquired pneumonia (CAP)	Lower respiratory tract infection with a new infiltrate in the Chest X-ray admitted from the community. In the Kristoffersen trial, chest X-ray signs of pneumonia were not required for inclusion in the study.
Hospital-acquired pneumonia	Lower respiratory tract infection with a new infiltrate in the Chest X-ray in a patient in a hospital setting for at least 48–72hours
Ventilator-associated pneumonia (VAP)	ICU patients intubated for mechanical ventilation for >48 h with all of the following criteria: 1) clinically diagnosed with a new or persistent infiltrate on chest radiography associated with at least two of the following: purulent tracheal secretions, temperature >38C or, leukocyte count >11,000 mL or ,3,000 mL
Exacerbation of asthma	Episodic symptoms of airflow obstruction, which are at least partly reversible, as assessed by lung-function tests
Exacerbation of chronic obstructive pulmonary disease (ECOPD)	Sustained worsening of the patient's condition, from the stable state and beyond normal day-to-day variations, that is acute in onset and necessitates a change in regular medication in a patient with underlying COPD; defined by post-bronchodilator spirometric criteria according to the GOLD-guidelines; in patients with a clinical history of COPD and smoking, lung function testing at the time of inclusion was not mandatory

Legend: ARI, acute respiratory infection; COPD, chronic obstructive pulmonary disease;

Extra web appendix 2. Kaplan Maier curves for the risk of mortality within 30 days of follow up overall and in different subgroups



Legend: A. Overall; B. Emergency department; C. Intensive care unit; D. community-acquired pneumonia; E. Exaceration of COPD; F. ventilator associated pneumonia.

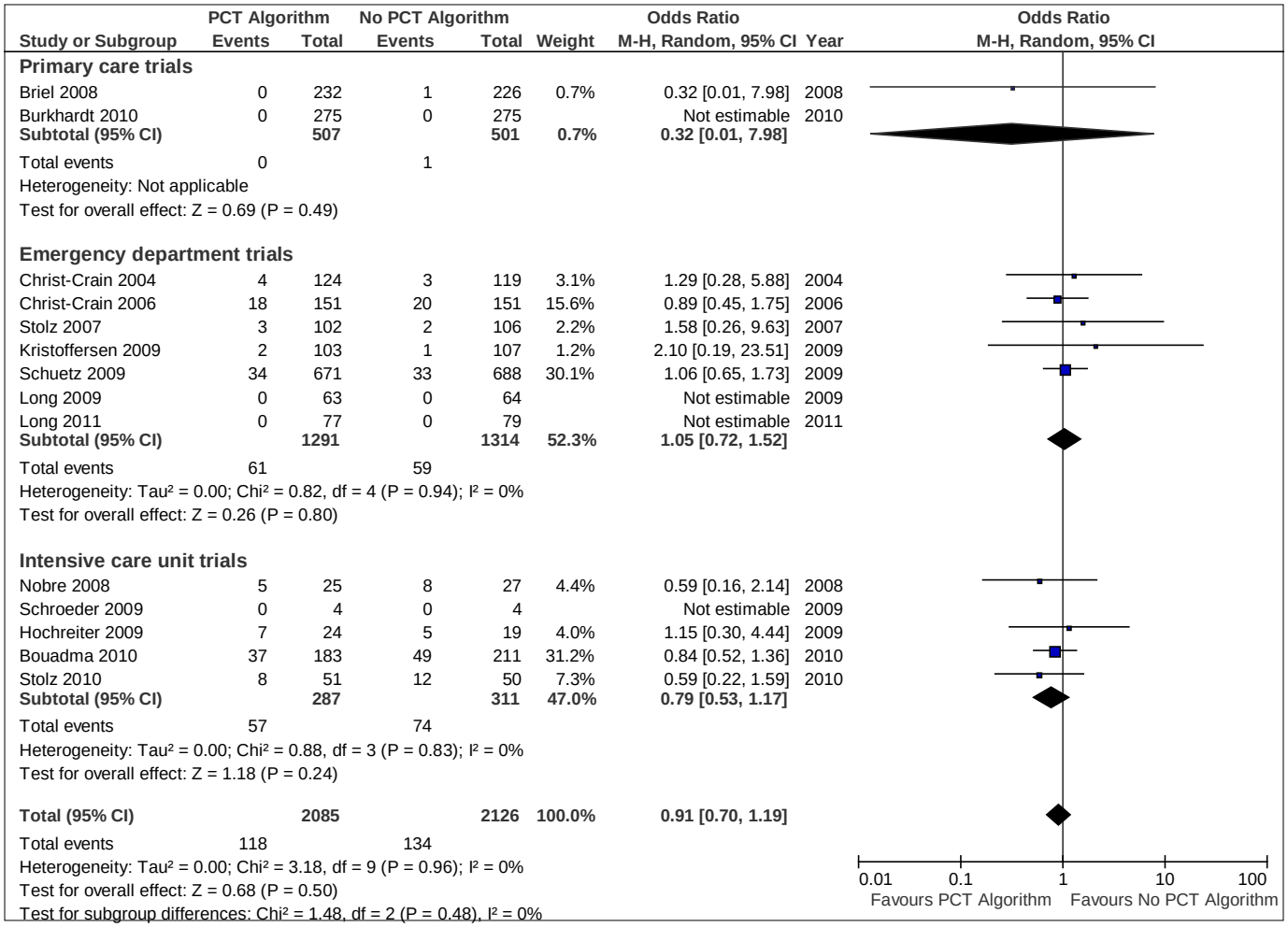
Extra web appendix 3. Sensitivity analyses

	PCT group	Control group	Adjusted OR (95%CI)[a]	*p for interaction**
Main analysis (assumption that patients lost to follow-up did not experience an event)				
Mortality	118/2085 (5.7%)	134/2126 (6.3%)	0.94 (0.71, 1.23)	
Treatment failure	398/2085 (19.1%)	466/2126 (21.9%)	0.82 (0.71-0.97)	
Assumption that patients lost to follow-up experienced an event (death or treatment failure)				
Mortality	47/1188 (4%)	44/1195 (3.7%)	0.97 (0.6, 1.55)	
Treatment failure	410/2085 (19.7%)	476/2126 (22.4%)	0.84 (0.72, 0.98)	
Exclusion of patients lost to follow-up (complete case analysis)				
30 days mortality	118/2072 (5.7%)	134/2116 (6.3%)	0.94 (0.71, 1.23)	
Treatment failure	397/2072 (19.2%)	466/2116 (22%)	0.83 (0.71, 0.96)	
Excluding the ProRATA trial [1]				
Mortality	81/1902 (4.3%)	85/1915 (4.4%)	0.97 (0.61, 1.55)	*0.81*
Treatment failure	361/1902 (19%)	417/1915 (21.8%)	0.84 (0.71, 0.98)	*0.94*
Excluding all ICU trials				
Mortality	61/1798 (3.4%)	60/1815 (3.3%)	0.97 (0.61, 1.55)	*0.55*
Treatment failure	341/1798 (19%)	392/1815 (21.6%)	0.84 (0.72, 1.00)	*0.88*
Excluding all trials with low adherence (<70%) or not reporting adherence				
Mortality	61/1478 (4.1%)	65/1486 (4.4%)	0.97 (0.61, 1.55)	*0.96*
Treatment failure	313/1478 (21.2%)	366/1486 (24.6%)	0.82 (0.69, 0.98)	*0.66*
Excluding all trials without allocation concealment				
Mortality	78/1489 (5.2%)	92/1534 (6%)	0.93 (0.59, 1.49)	*0.72*
Treatment failure	312/1489 (21%)	357/1534 (23.3%)	0.85 (0.72, 1.02)	*0.43*
Excluding all trials without blinded outcome assessment				
Mortality	74/1463 (5.1%)	85/1506 (5.6%)	0.93 (0.59, 1.49)	*0.87*
Treatment failure	312/1463 (21.3%)	358/1506 (23.8%)	0.85 (0.71, 1.01)	*0.47*
Excluding all trials with no follow up beyond hospital discharge				
Mortality	109/1954 (5.6%)	128/1996 (6.4%)	0.97 (0.6, 1.55)	*0.25*
Treatment failure	383/1954 (19.6%)	455/1996 (22.8%)	0.82 (0.71, 0.96)	*0.26*

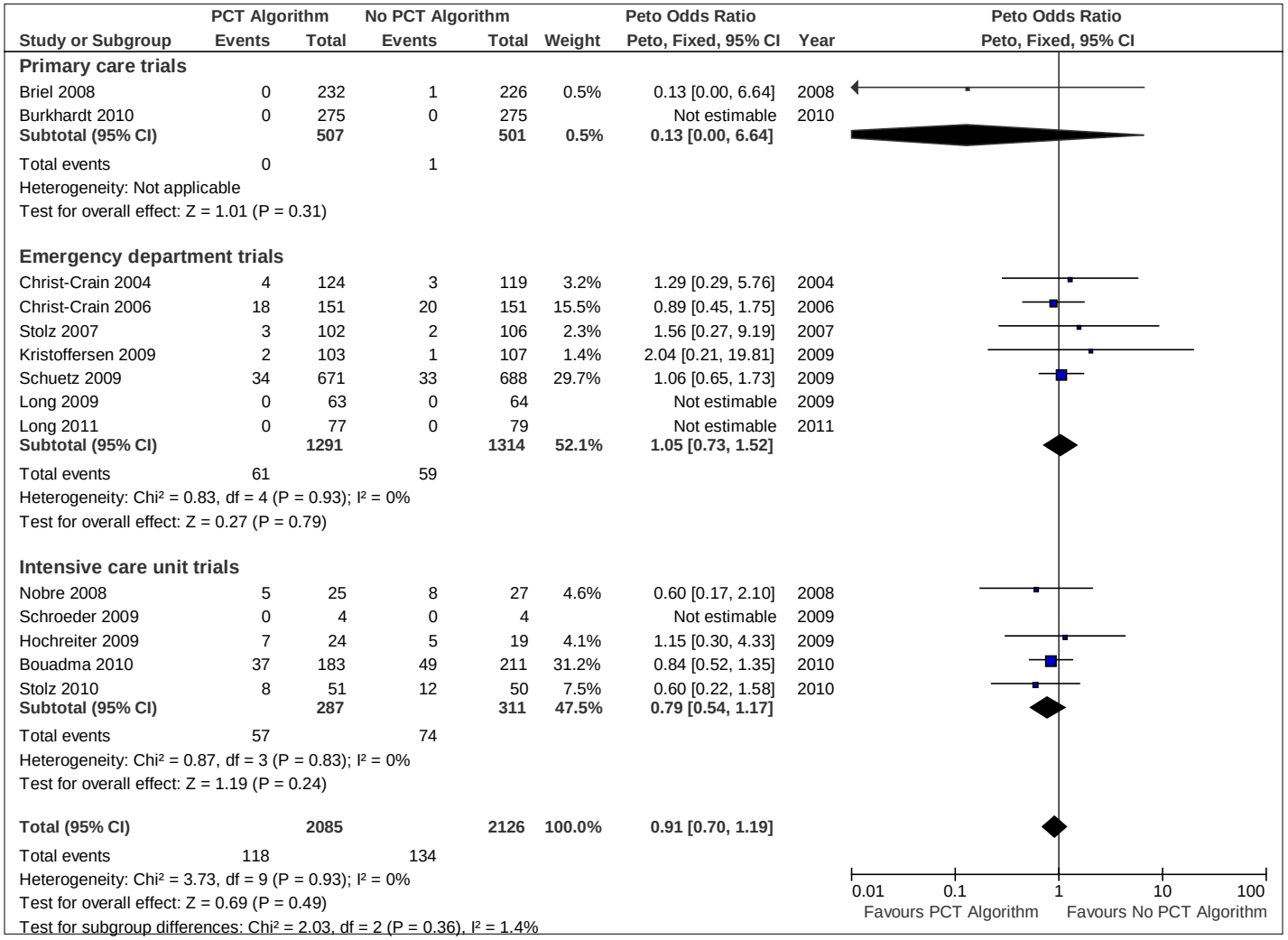
*Legend: *Analyses with individual patient data from all trials and added interaction terms (e.g. low adherence x PCT group) in the regression model to test for effect modifications. P-values <0.05 indicate evidence for effect modification.* [1] *Bouadma L, Luyt CE, Tubach F, et al. Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a multicentre randomised controlled trial. Lancet. 2010;**375:**(9713):463-74.*

Extra web appendix 4. Further sensitivity analyses using meta-analysis with aggregated data (no covariable adjustment) to investigate heterogeneity

Overall Mortality by Clinical Setting, Mantel-Haenszel random effects

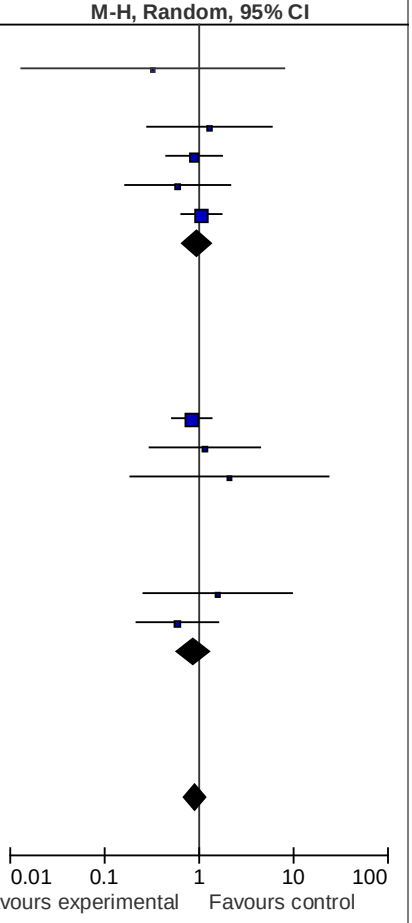


Overall Mortality by Clinical Setting, Peto fixed effects

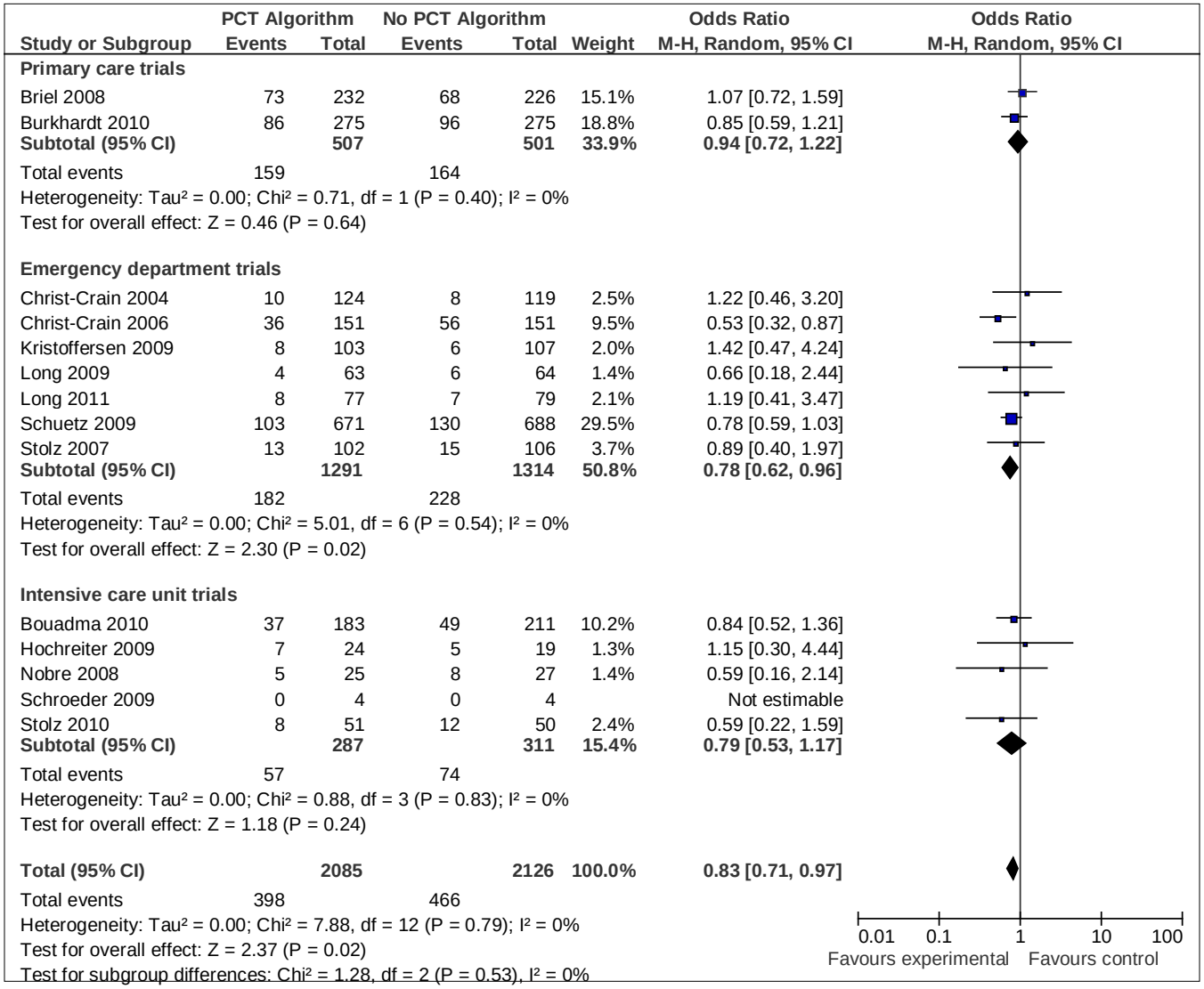


Overall Mortality by Adherence, Mantel-Haenszel random effects

Study or Subgroup	PCT Algorithm Events	PCT Algorithm Total	No PCT Algorithm Events	No PCT Algorithm Total	Weight	Odds Ratio M-H, Random, 95% CI
Adherence to PCT Algorithm >70%						
Briel 2008	0	232	1	226	0.7%	0.32 [0.01, 7.98]
Burkhardt 2010	0	275	0	275		Not estimable
Christ-Crain 2004	4	124	3	119	3.1%	1.29 [0.28, 5.88]
Christ-Crain 2006	18	151	20	151	15.6%	0.89 [0.45, 1.75]
Nobre 2008	5	25	8	27	4.4%	0.59 [0.16, 2.14]
Schuetz 2009	34	671	33	688	30.1%	1.06 [0.65, 1.73]
Subtotal (95% CI)		**1478**		**1486**	**54.0%**	**0.96 [0.66, 1.38]**
Total events	61		65			
Heterogeneity: Tau² = 0.00; Chi² = 1.33, df = 4 (P = 0.86); I² = 0%						
Test for overall effect: Z = 0.24 (P = 0.81)						
Adherence to PCT Algorithm <70% or not available						
Bouadma 2010	37	183	49	211	31.2%	0.84 [0.52, 1.36]
Hochreiter 2009	7	24	5	19	4.0%	1.15 [0.30, 4.44]
Kristoffersen 2009	2	103	1	107	1.2%	2.10 [0.19, 23.51]
Long 2009	0	63	0	64		Not estimable
Long 2011	0	77	0	79		Not estimable
Schroeder 2009	0	4	0	4		Not estimable
Stolz 2007	3	102	2	106	2.2%	1.58 [0.26, 9.63]
Stolz 2010	8	51	12	50	7.3%	0.59 [0.22, 1.59]
Subtotal (95% CI)		**607**		**640**	**46.0%**	**0.86 [0.58, 1.28]**
Total events	57		69			
Heterogeneity: Tau² = 0.00; Chi² = 1.70, df = 4 (P = 0.79); I² = 0%						
Test for overall effect: Z = 0.74 (P = 0.46)						
Total (95% CI)		**2085**		**2126**	**100.0%**	**0.91 [0.70, 1.19]**
Total events	118		134			
Heterogeneity: Tau² = 0.00; Chi² = 3.18, df = 9 (P = 0.96); I² = 0%						
Test for overall effect: Z = 0.68 (P = 0.50)						
Test for subgroup differences: Chi² = 0.14, df = 1 (P = 0.70), I² = 0%						



Treatment Failure by Clinical Setting, Mantel-Haenszel random effects



Treatment Failure by Adherence, Mantel-Haenszel random effects